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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/062,197

Applicant(s)

CHEN ET AL

Examiner

Michael Borin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08/24/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 8-16 and 20-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 17-19, 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/24/2005 has been entered.

Status of Claims

2. Claims 1-29 are pending. Claims 8-16,20-28 withdrawn from further consideration. Claims 1-7,17-19,29 are under consideration.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-7,17-19,29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.

A. Claim 1, line 3: It is not clear, what is being "exposed to or labeled with" fluorophores: the "specimen", or the "specimen field".

B. Claim 1, lines 11 and 14: it is not clear which "each location" is being addressed.

C. Claim 1, "acquiring" steps: The claim addresses two acquiring steps, one for the first wavelength, and another for the second. While the latter is addressed as being acquired "at a high magnification", it is unclear which magnification is to be used for the former acquiring step: high, as for the subsequent step, or "low" as for the preceding step.

Claim Rejections - 35 USC § 102 and 103.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claim 1 is rejected under 35 U.S.C. 102(e) as anticipated by Dunlay et al (US Patent 6,573,039)

The instant claims are directed to method for detecting a target body (i.e., cell, virus, molecule, etc) wherein the target is labeled with two fluorophores, its location is registered, first, by scanning at low magnification, then fluorescent images produces by first and second fluorophore, indexing first and second image, and inspecting first and second images for the presence of the target.

Dunlay describes use of two fluorescent labels to identify translocation of a protein of interest (i.e., target body) from nucleus of a cell to cytoplasm. A sample is loaded with two fluorescent labels, one- for the protein of interest, and another - to define individual cells. See, for example, Example 1. Other fluorescent labels can be used alternatively. Col. 4, lines 6-34. The sample is prescanned to identify an area for focusing (col. 5, lines 55-65), and fluorescent images of the two fluorescent labels are acquired. The image of the second fluorophore indicating location of the cell nucleus is used to calculate NetCyt Difference image which is difference between cytoplasmic and nuclear fluorescent probes (i.e., and indexed image). See examples 1 or 2, and claims 7-15. Thereby, the presence of the protein of interest (i.e., target body) is detected.

Note that the first scanning step, addressed as scanning for sources of photons at the first and second wavelengths is understood as simply preliminary scanning the specimen because, as the specimen contains two fluorophores, it is thus, a source of photons at the first and second wavelengths.

Further, with respect to the limitation of acquiring first and second images using a filter that blocks the unwanted fluorescence, any fluorescent microscope, such as

Zeiss Axiovert used in Dunlay et al, is equipped with a filter to selectively detect fluorescence at a desired wavelength.

5. Claims 1-7,17-19,29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunlay et al (US Patent 6,573,039).

The reference is applied as addressed in the previous rejection. The rejection above addressed just one use of the computer controlled optical system described in Dunlay for detection of a protein of interest in a sample loaded with two fluorophores. The references teach that a wide variety of different fluorescent labels can be alternatively used (col. Lines 6-41), and that the methods of determining a variety of cell parameters using such method are well known in the art (columns 1-2). It would be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to use the computer controlled optical system described in Dunlay for detection of any "target body" of interest, such as cells, microorganisms, etc. One would have reasonable expectation of success that using a proper combination of fluorophores from those well known in the art would permit identification of other "target bodies" of interest. Further, selection of details of detection "target bodies", such as methods of selecting and preparing samples and imaging, addressed in the dependent claims, are well known in the art and will be obvious to an artisan as a result of routine optimization.

6. Claims 1-7,17-19,29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kirchanski et al (US 4581334) in view of Mason et al.

US 4581334 teaches method of detection of a target body (phagocyte cells) comprising the steps of obtaining a specimen (blood sample with phagocytes) loaded with two fluorescent labels, identifying the cells on the basis of light scatter characteristics (i.e., scanning the specimen at low magnification for cells, i.e., for sources of photons at first and second wavelengths), registering location of the cells, detecting fluorescence intensity at two wavelengths, and forming the ratio of fluorescence intensity at two wavelengths (i.e., indexing fluorescence). See claims 1-8.

The reference does not teach acquiring fluorescent images; rather it teaches photometric method of acquiring fluorescence at two wavelengths. The 4,581,334 patent was issued at 1986, i.e., at the time when imaging technology has not been developed yet. However, as digital fluorescent imaging and methods of cell image acquisition have been later developed, it was demonstrated that fluorescent imaging methods are superior to photometric in that they are more sensitive, provide better temporal, as well as spatial resolution, and eliminate artifacts due to probe localization, cell geometry and cell movement. See, for example, Mason et al; pages 164-169. Therefore, it would be *prima facie* obvious to one skilled in the art at the time the invention was made, to replace photometric way of detecting fluorescence by detecting fluorescence intensity at two wavelengths with acquiring fluorescence images at two wavelengths as the latter technique provides more sensitivity and spatial resolution which are a desirable result for an analytical method.

Further, selection of details of detection "target bodies", such as methods of selecting and preparing samples and imaging, addressed in the dependent claims, are well known in the art and will be obvious to an artisan as a result of routine optimization.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb